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The Effectiveness of Boiled Rosy Periwinkle (*Catharanthus roseus*) in Decreasing SGOT and SGPT Value of Male Wistar Strain Rats with Acute Hepatitis Model

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ABSTRACT

Acute hepatitis is a disease that attacks the liver and causes inflammation in the liver cells which is characterized by swelling, damage, death, and even disruption of liver function, so that it can result in increased values of Serum Glutamic Pyruvic Oxaloactic Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT). This study aims to determine the effectiveness of the Rosy Periwinkle (Catharanthus roseus) on decreasing SGOT and SGPT levels. The object of this research is 30 male Wistar strain rats aged 2-3 months with a weight of 180-200 grams which were adapted for 7 days. The object of this study was divided into 3 groups, namely the treatment group, the positive control group and the negative control group. The treatment group and positive control group were induced Paracetamol 120 mg / day orally for 7 days. 5.2 grams of boiled Rosy Periwinkle (Catharanthus roseus) as much as 3.6 cc orally for 7 days was given to the treatment group. Data were analyzed with SPSS version 24, One Way ANOVA test to compare SGOT and SGPT values. The results of this study found that there was a significant difference in the SGOT value between; the treatment group, the positive control group and the negative control group ($p < 0.05$) and there were significant differences in the SGPT value between the treatment group and the positive control group ($p < 0.05$). The conclusion of this study is that the boiled Rosy Periwinkle (Catharanthus roseus) has an effect on the decrease in SGOT and SGPT values in the male wistar strain of Rats with acute hepatitis model.

Keywords: Paracetamol, SGOT, SGPT , Catharanthus Oseus

INTRODUCTION

The prevalence of acute hepatitis by HBsAg examination carried out on blood donor group, there are about 2.50 to 36.17 in Indonesia. Hepatitis is the most common diseases in Indonesia, with the result that the high prevalence of hepatitis causing post-acute problems even cause cirrhosis hepatitis and primary hepatocellular carcinoma, 10% of hepatitis virus infections can cause chronic hepatitis and there are 20% with patients with chronic hepatitis will cause cirrhosis hepatitis and hepatocellular carcinoma within 25 years of contracting

hepatitis. About 350 million people with hepatitis are recorded in the world and around 220 million (78%) of Indonesia's population are suffering hepatitis (Helilintar , Rochana, Aswi, 2017).

Epidemiological data shows that there is little intention by the public to come to the health services compared to those suffering acute hepatitis. Hepatitis is a chronic disease and almost everyone has hepatitis. Healthy conditions still do not show symptoms and signs but the disease is will continuously contagious (Indonesian Ministry of Health, 2014) .

People in Indonesia, who are rich with herbal plants, believe in the treatment by using herbal ingredients more because they are relatively inexpensive. One method that is often done by the public is by boiling the herbals (Sudharmono, 2014).

Therefore, researchers are interested in conducting research on the effect of Rosy Periwinkle (Catharanthus Roseus) decoction in decreasing levels of SGOT and SGPT enzymes in male wistar strain rats with acute hepatitis models.

LITERATURE REVIEW

The liver is the largest organ located at the top right of the cavity abdomen. The liver has dark red look because it contains a lot of blood, weight of liver is approximately 1.5 kg. the Liver has four lobes including dextra lobes, caudate lobes, sinistra lobes, and quadatus lobes. Besides, the liver has several functions such as carbohydrates metabolism in changing galactose and fructose to glucose, further it also function as fat metabolism by storing backup convert fat into energy for the body's functions.

And protein metabolism by removing ammonia from body fluids through the formation of ureum. And other functions is as a place for storing vitamins, storing iron and storing ferritin. It also acts as a coagulation of blood in large quantities so that the liver can excrete drugs and other hormones. The liver also has a very important role it acts to neutralizing poison, because the liver acts as a biotransformation that converts harmful substances or poisons into harmless substances. Therefore, the liver is prone to liver damage and especially damage to cells liver cells resulting in an increase in levels of the enzyme of SGOT (Serum Glutamate Oxaloacetate Transaminase) and levels of SGPT (Serum Glutamate Pyruvate Transaminase) enzyme. There are two cells in the liver, namely hepatocyte cells and macrophage cells which are often referred to as Kuepfer cells and Ito cells. The Ito cells act as lipid accumulation,

while hepatocyte cells are cells in the liver lobules of these cells forming 1-2 cells similar to the shape of a brick (Agung , Nugraha, Sri , et al , 2018) .

Hepatitis is a disease that causes inflammation in the liver. Caused by a virus infection. The viruses are hepatitis A, B, C, D and E. Hepatitis that lasts less than 6 months is called "acute hepatitis". We can see signs and symptoms such as fatigue, nausea, decreased appetite, pain in the liver, pale stools, and weight loss without cause. Other causes are by consuming alcoholic beverages, excessive consumption of drugs and exposure to toxins. But acute hepatitis has not a high risk, it cannot make inflammation in the liver in a long period of time and can also recover by its own. While hepatitis that lasts for more than 6 months is called "chronical hepatitis". Signs and symptoms of chronic hepatitis such as feeling faint pain (malaise), worsening appetite, and often feels tired. This chronic hepatitis can cause it to occur chronic liver disease or cirrhosis. It includes the enlargement of the spleen, the presence of small blood vessels shaped like a spider's web that looks on the skin, the accumulation of fluid in the stomach (ascites), and reddish palms. (Yudhasmara, 2015) .

Paracetamol is the most common drug used to reduce fever. Fever is one of the signs and symptoms of acute hepatitis. In this study, the researcher used paracetamol as an ingredient to be injected in male Wistar strain rats with acute hepatitis model. Acetaminophen or paracetamol (N-acetyl-paraaminophenol or APAP) is a type of antipyretic drug that is widely used in the world. The use of this paracetamol at the age of 0-5 months are 20%, while at the age of 6-11 months by 28%. Paracetamol can actually cause acute liver failure either accidentally or intentionally. Many deaths caused by paracetamol, in the United States, 2,600 people are hospitalized and about 500 people died. A case report on patients who were immediately postoperatively given paracetamol intravenously after 12 hours of administration symptoms of vomiting, nausea, anoxeria, confused and agitation. After that, liver function examination was found to be an increase in transaminase serum 10 times above normal. Even though high doses produced by the paracetamol have a link to the risk of liver failure, however, long-term use of the paracetamol with standard doses can be risk of acetaminophen hepatotoxicity (Yusri, Sayoeti, Marlia, 2015).

Excessive use of paracetamol or long time consumption will cause overdose, with this overdose hepatic cell necrosis in the area of Centro lobules can cause acute liver failure.GSH (Glutathion-SH) contained in liver cells susceptible to injury by the presence of liver oxidant. With the use of excessive doses also cause compounds that are toxic NAPQI (N-acetyl-p-benzokuinon) that cannot be neutralized through glutathione, so that free radical

reactions occur with the effects caused by the liver organ damage function. The levels of the SGOT (Serum Glutamate Oxaloacetate Transaminase) and SGPT (Serum Glutamate Pyruvate Transaminase) enzymes are indicators in carrying out diagnostic tests for damage that occurs in liver cells. (Rafita, Lisdiana, Marianti, 2015)

Periwinkle or *Catharanthus roseus* (Apocyanaceae) is a herbal plant, in Indonesia well-known as *Vinca rosea* or *lachnera rosea* and *Ammocallis Rosea.* Rosy Periwinkle have different names each country in Indonesia, known as *tapak dara,rutu-rutu,kembang sedadu*, in England known as *Madagascar periwinkle, rose periwinkle* , in Malay it is called *kemunting cina* , in Vietnam it is called *hoa hai dang*, in the Philippines it is called *tsitsirika* , and in China it is known by the *name chang chun hua.* The rosy periwinkle plant has been used by some countries such as Indonesia, India , BRA zilcook Islands, Dominican Republic, England, Jamaica, Mozambique, Pakistan, Taiwan, Thailand, and Nigeria. This tread plant originates from the United States and generally grows as an ornamental plant. This plant can grow in tropical climates, and grows in the lowlands about 800 meters above sea level (Nyoman , Iwan, Made, et al , 2015).

Rosy Periwinkle (*Catharanthus Roseus*) has a height of around 120 cm. The leaf of Rosy Periwinkle (*Catharanthus Roseus*) is arranged face to face and the tread flower (*Catharanthus Roseus*) grows under small leaves at a glance like a pigeon palm so it is often nicknamed by pigeon palms. It has thick, glossy green leaves with ovoid shape. Dara (*Catharanthus Roseus*) has flowers consisting of 5 petals that grow on the stalk or in each armpit of the leaf. This plant can be propagated or can grow with seeds, stem cuttings, or roots. Purplish red flowers and in some type also has a white color. (Tana man medicine, 2014)

Rosy periwinkle (*Catharanthus roseus*) containing glycosides, alkaloids, terpenoids, Flavonoid, and phenolic that can be used as a medicine. Traditional medicine has long been known and applied by our society, especially ingredients from herbal plants . (Rahma, Hakim, Sri.2017)

Rosy periwinkle (*Catharanthus roseus*) has been shown to have many benefit, such as for diabetes mellitus, painful urination, hepatitis, stones kidney, hypertension, breast cancer bronchitis, asthma, fever, malaria, lack of blood, dysentery, burns, swelling thrush, constipation, irregular menstruation, bleeding due to decreased platelets. (Abednego, 2016: p. 337)

The damage that occurs in the liver cells can lead to increased levels of the SGOT (Serum Glutamic Oxaloacetate transaminase) and S GPT (serum glutamate pyruvate transaminase) enzyme in the liver. The increase of the enzyme is caused by frequent consumption of certain

drugs such as statins that are used to control cholesterol, consuming alcohol, autoimmune, cirrhosis, thyroid dysfunction, excess iron in the body. With this increase, an examination is carried out by measuring the levels of the SGOT (Serum Glutamate Oxaloacetate Transaminase) and SGPT(serum glutamate pyruvate transaminase) enzyme. SGOT (Glutamate Oxaloacetate serum transaminases) present in the liver organ, the heart organ, skeletal muscles, kidney and it show as big numbers. SGPT (serum glutamate pyruvate transaminase) is derived from liver. Although the levels of the SGOT (Serum Glutamate Oxaloacetate Transaminase) and SGPT (Serum Glutamate Pyruvate Transaminase) enzyme is not a sign of impaired liver function, but both of these enzyme levels are often used as *screening* enzymes which are parameters in following *up* on making a diagnosis (Marlia, Mulyadi, Enny, 2016).

METHODS

This research is an experimental laboratory research. The object of this study were 30 male wistar stain rats weighing 180-200 grams at age of 2-3 months, the subject then divided into three groups namely the negative control group (given food and drink as usual), positive control group (given food, drink as usual and the liver was damaged with paracetamol 120 mg / day) and the treatment group (the liver was tampered with paracetamol as much as 120 mg / day and given rosy periwinkle (Catharanthus roseus) decoction with a weight of 5.2 grams in 100 cc and given as much 3.6 cc orally for 7 days, in 12 hours of light and 12 hours of darkness, the weight of rats with manage to not change for ± 10% for 7 days of adaptation.

Making Rosy Periwinkle Decoction

Rosy periwinkle (Catharanthus roseus) is taken from Parongpong , West Bandung . The research was conducted in July 2019, the part of the plan that was taken is the leaves, flowers, stems and roots. This research use purple colored flowers of rosy periwinkle. Dried rosy periwinkle weighing 5.2 grams then boiled in 300 cc of water for 9.30 seconds until the cooking water becomes 100 cc. Then the cold boiled water is given to objects as much as 3.66 cc for 7 days.

The way to damage the liver, Wistar strain rat with acute hepatitis model was injected paracetamol of 120 mg / day for 7 days as indicated by increasing the value of the levels of the SGOT (Serum Glutamic Oxaloacetate transaminase) and the levels of enzyme SGPT (Serum glutamate pyruvate transaminase) enzyme. The treatment was given to positive

control group and treatment groups so that the laboratory examination was conducted in different time.

Research Procedure

The object of the study was 30 male Wistar strain rats, which were adapted for 7 days (12 hours of light and 12 hours of dark). The rats were divided into 3 groups, each group consisted of 10 male Wistar strain rats, namely:

negative groups (given food and drink as usual)

1. positive group (given eat, drink as usual and the liver damaged by using paracetamol as much as 120mg / day)
2. treatment group (the liver was destroyed using paracetamol 120 mg / day and given water therapy of rosy periwinkle (Catharanthus Roseus) decoction as much as 5.2 g in 300 cc water and given as much as 3.66 cc for 7 days).

From the 8th to 15th, the liver of positive group and the treatment group was marred using 120 mg / day paracetamol for 7 days. In the 15th day of the examination to the levels of the SGOT (Serum Glutamic Oxaloacetate transaminase) and SGTP (Serum Glutamate Pyruvate Transaminase) enzyme was conducted in order to find the results of the pre-test, while the treatment group was still administering therapeutic boiling water of Rosy periwinkle (Catharanthus Roseus) as much as 5.2 g in 300 cc of boiling water given as much as 3.6 cc in 7 days. In the 22nd day, the researchers conducted another laboratory check to assess the level of SGOT (Serum glutamic Oxaloacetate transaminase) and SGPT (Serum glutamate pyruvate transaminase) enzyme in the liver as a result of post tes. The calculation was performed using SPSS version 24 test one way ANOVA. This test is used to compare the results of the SGOT (Serum Glutamate Oxaloacetate Transaminase) and SGPT (Serum Glutamate Pyruvate Transaminase) enzyme levels in the liver of the male wistar strain rats

RESULTS

The results of calculating the levels of SGOT (Serum Glutamate Oxaloacetate Transaminase) and SGPT (serum Glutamate Pyruvate Transaminase) enzymes using the One Way ANOVA test before and after the water treatment of Rosy Periwinkle (catharanthus Roseus) in male wistar rats with acute hepatitis models can be seen in the following table

Table 1. **The levels of SGOT enzymes using the One Way ANOVA**

Dependent Variable	(I) GROUPS	(J) GROUP	95% Confidence Interval	
			Lower Bound	Upper Bound
SGOT_PRE	1.00	2.00	-238.5440	-172.0960
		3.00	-223.7190	-157.2710
	2.00	1.00	172.0960	238.5440
		3.00	-18,3990	48.0490
	3.00	1.00	157.2710	223.7190
		2.00	-48.0490	18,3990
SGOT_POST	1.00	2.00	-999.3461	-927,1139
		3.00	-103.8861	-31.6539
	2.00	1.00	927,1139	999.3461
		3.00	859.3439	931.5761
	3.00	1.00	31.6539	103.8861
		2.00	-931.5761	-859.3439
SGPT_PRE	1.00	2.00	-105.9032	-61.4368
		3.00	-129.5132	-85.0468
	2.00	1.00	61,4368	105.9032
		3.00	-45.8432	-1.3768
	3.00	1.00	85.0468	129.5132
		2.00	1.3768	45.8432
SGPT_POST	1.00	2.00	-1030.8705	-941.8695
		3.00	-74.1405	14,8605
	2.00	1.00	941.8695	1030.8705
		3.00	912.2295	1001,2306
	3.00	1.00	-14.8605	74,1405
		2.00	-1001.2306	-912.2295

* The mean difference is significant at the 0.05 level.

The levels of SGOT (Serum Glutamate Oxaloacetate Transaminase) and SGPT (Serum Glutamate Pyruvate Transaminase) enzyme are cells that are present in the liver, with the highest levels of SGPT (Serum Glutamate Pyruvate Transaminase) enzymes find in the liver. If there is cell damage in the liver, a lot number of enzymes will go out into the extra cell space and into the bloodstream (Hartono Kahar, 2017).

The levels SGOT (Serum Glutamate Oxaloacetate Transaminase) and SGPT (Serum Glutamate Pyruvate Transaminase) enzymes was assessed twice. The examination was

carried out before and after the water treatment of rosy periwinkle (*Chatharanthus Roseus*) decoction in the male wistar strain rats with acute hepatitis model.

Measurement results of statistical test comparison using SPSS version 24, one-way ANOVA test, this was done to compare levels of SGOT (Serum Glutamate Oxaloacetate Transaminase) and levels of SGPT (Serum Glutamate Pyruvate Transaminase) before and after given boiling water therapy of rosy periwinkle (Catharanthus Roseus) in male Wistar strain rats with acute hepatitis model. The results of the analysis are as follows:

Table 2. **Results of data analysis on the value of SGOT (Serum Glutamate Oxaloacetate Transaminase) enzyme levels on day 15 before treatment of boiled water od rosy periwinkle (*Catharanthus Roseus*) in male wistar strain with acute hepatitis model.**

Dependent Variable	(I) GROUPS	(J) GROUP	Mean Difference (IJ)	Std. Error	Sig.
SGOT_PRE	1.00	2.00	-205.32000*	13,99992	.000
		3.00	-190.49500*	13,99992	.000
	2.00	1.00	205.32000*	13,99992	.000
		3.00	14,82500	13,99992	.518
	3.00	1.00	190.49500*	13,99992	.000
		2.00	-14,82500	13,99992	.518

From table 1, the results obtained from the calculation of SGOT levels (Serum Glutamate Oxaloacetate Transaminase) with a comparison between group 1 (negative control group), group 2 (positive control group) and group 3 (treatment group) obtained significant results ($p < 0.05$). Examination was carried out on the 15th day before being given boiled water therapy of rosy periwinkle (Catharanthus Roseus) which was given as much as 3.6 cc orally within 7 days in male Wistar strain rats that had been induced by paracetamol as much as 120mg / day given for 7 days per day orally. While the comparison between group 2 (positive control group) and group 3 (treatment group), the results of the examination of SGOT (Serum Glutamate Oksaloacetat Transaminase) levels increased, this was due to the induction of paracetamol as much as 120 mg / day for 7 days orally with 7 the presence of paracetamol can damage liver function or disrupt liver function in male wistar rats with acute hepatitis

model. So that there is no significant result (p <0.518) between group 2 (positive control group) and group 3 (treatment group).

Table 3. **The results of data analysis on the value of the SGOT (Serum Glutamate Oxaloacetate Transaminase) enzyme on day 22 after treatment of boiled water of rosy periwinkle (*Catharanthus Roseus*) in male wistar strain rats with acute hepatitis model.**

SGOT_POST	1.00	2.00	-963.23000 *	14,56636	.000
		3.00	-67.77000 *	14,56636	.000
	2.00	1.00	963.23000 *	14,56636	.000
		3.00	895.46000 *	14,56636	.000
	3.00	1.00	67.77000 *	14,56636	.000
		2.00	-895.46000 *	14,56636	.000

In table 2 above, the results of calculating the SGOT (Serum Glutamate Oxaloacetate Transaminase) enzyme levels after administration of water therapy from rosy periwinkle (Catharanthus Roseus) with a weight of 5.2 grams and as much as 3.6 cc were given for 7 days orally. Between group 1 (negative control group) with group 2 (positive control group) and group 3 (treatment group) obtained significant results (p <0.05). This is because in group 1, only given food and drink as usual but not induced by paracetamol. Therefore in group 2 (positive group) given food and drink as usual then induced by paracetamol as much as 120 mg / day orally for 7 days and not treated by boiled water therapy of rosy periwinkle (Catharanthus Roseus), the result shows that SGOT (Serum Glutamate Oksaloacetate) enzyme levels increase. In group 3 (the treatment group) shows that the SGOT enzyme (Serum Glutamate Oksaloacetate Transaminase) decreased, it was due to the provision of boiling water therapy of rosy periwinkle (Catharanthus Roseus) as much as 3.6 cc with a leaf weight of 5 , 2 gr and given orally for 7 days in male Wistar strain rats with an acute hepatitis model, so that a comparison between group 2 (positive control group) and group 3 (treatment group) obtained significant results (p <0.05). It was concluded that by administering 3.6 tc boiled tap water (Catharanthus Roseus) with a weight of 5.2 g administered orally for 7 days make the levels of SGOT (Serum Glutamate Oxalacetate Transaminase) were approaching normal levels.

Table 4. **The results of data analysis on the value of SGPT (Serum Pyruvate Oxaloacetate Transaminase) enzyme on the 15th day before giving boiled water treatment therapy of rosy periwinkle (*Catharanthus Roseus*) in male wistar strain rats with acute hepatitis model.**

SGPT_PRE	1.00	2.00	-83.67000 *	8.96710	.000
		3.00	-107.28000 *	8.96710	.000
	2.00	1.00	83.67000 *	8.96710	.000
		3.00	-23.61000 *	8.96710	.036
	3.00	1.00	107.28000 *	8.96710	.000
		2.00	23.61000 *	8.96710	.036

Table 3 shows the comparison of SGPT enzyme levels before giving boiled water therapy between group 1 (negative control group) and group 2 (positive control group) and group 3 (treatment group) obtained significant results (p <0.05). In group 1 (negative control group) the results of SGPT (Serum Glutamate Pyruvate Transaminase) were in the normal limits, due to the absence of 120 mg / day of paracetamol induction given orally for 7 days. Different with the results in group 2 (positive control group)) and group 3 (the treatment group) that show a insignificant results (p <0.036). This is because in group 2 (the positive control group) and the group 3 (the treatment group) were induced by paracetamol as much as 120 mg / day orally for 7 days. That process damaged the liver of group 2 (positive control group) and group 3 (treatment group) in male wistar rats with acute hepatitis model and caused the levels of the SGPT enzyme (Serum Glutamate Pyruvate Transaminase) elevated. Increased levels of the enzyme SGPT (Serum Glutamate Pyruvate Transaminase) are caused by the administration of paracetamol as much as 120 mg / day given orally for 7 days in male wistar strain rats. Paracetamol is a drug that is included in the antipyretic group by working to overcome pain, fever, and toxicity. The presence of paracetamol can work in the formation of toxic reactive metabolic and free radicals through the biotransformation process by cytochrome p450 enzymes with the help of CYP2E1 isozymes. (Sri Oktavia, Ifora, et al., 2017).

Table 4. **The results of data analysis on the value of SGPT (Serum Piruvate Oxaloacetate Transaminase) enzymes on day 22 after treatment of rosy periwinkle (*Catharanthus Roseus*) decoction in male wistar strain of acute hepatitis model.**

SGPT_POST	1.00	2.00	-986.37000 *	17,94798	.000
		3.00	-29.64000	17,94798	.242
	2.00	1.00	986.37000 *	17,94798	.000
		3.00	956.73000 *	17,94798	.000
	3.00	1.00	29.64000	17,94798	.242
		2.00	-956.73000 *	17,94798	.000

From table 4, the results of the calculation of SGPT (Serum Glutamate Pyruvate Transaminase) levels after being given boiled water therapy of rosy periwinkle (Chatharanthus Roseus) were given as much as 3.6 cc orally for 7 days. The result of comparing SGPT levels (Serum Glutamate Pyruvate Transaminase) in group 1 (negative control group) with group 2 (positive control group) showed a significant results ($p < 0.05$). This is because in group 1 (negative control group) only given food and drink as usual and in the group 2 (positive control group) were given food and drink as usual and the liver was damaged by giving induction of paracetamol as much as 120 mg / day orally and given for 7 days in male Wistar strain rats with acute hepatitis model. So that on the 22nd day checking was conducted and the results show the levels of SGPT (Serum Glutamate Pyruvate Transaminase) increased. While in group 1 (negative control group) compared with group 3 (treatment group), the result was not significant ($p < 0.242$). This happen Because in group 3 (treatment group), 120 mg / day of paracetamol was given orally and also get water therapy of rosy periwinkle (Catharanthus) Roseus) for 7 days. So the SGPT (Serum Glutamate Pyruvate Transaminase) results are close to normal values.

DISCUSSION

Conclusion

Rosy periwinkle (*Catharanthus roseus*) with a weight of 5.2 g leaves are boiled in the remaining of 300 cc to 100 cc of water is given as water therapy as much as 3.6 cc orally for 7 has an effects in decreasing the levels of SGOT (Serum Glutamate Oxaloacetate Transaminase) and SGPT (Serum Glutamate Pyruvate Transaminase) enzyme in male wistar strain rats with acute hepatitis model.

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